REMARKS

Status of the Claims

Claims 1, 4, 6–11, 13–15, 37–47 were pending in the present application.

Claims 1, 4, 6–11, 13–15, 37–47 were rejected.

By way of this amendment, new claims 48-53 have been added.

Upon entry of this amendment, claims 1, 4, 6–11, 13–15, 37– 53 will be pending.

Summary of the Amendment

New claim 48-53 have been added to refer to embodiments of the invention. . Support for the amendment appears throughout the specification and claims as filed.

No new matter has been added.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1, 4, 6–11, 13–15 and 37–47 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. The Office alleges that the claims contain subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the art that the inventors, at the time of the application was filed, had possession of the claimed invention. Applicants respectfully disagree.

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to

> show the applicant was in possession of the claimed genus.
>
> …
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is a substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.
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> …
>
> What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., Eli Lilly. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces.

MPEP § 2163(II)(A)(3)(a)(ii)(citations omitted).

Applicants respectfully note that the listed species adequately represent the genus of differentiation-specific antigens. Applicants have claimed ***a method of detecting the presence of a disseminated epithelial cell*** whereby CD34+ cells are eliminated from a sample and the presence of mRNA epithelial markers. A representative number of species which are sufficient diverse have been provided to establish that Applicants were in possession of the claimed invention at the time the application was filed. Those skilled in the art recognize the term "epithelial cell marker" and based upon the disclosure would

conclude that Applicants were in possession of the claimed invention at the time the application was filed.

The Office asserts that "Applicants have adequately described only 26, or less than 0.2%" of the members of the genus (Office Action, p.8). The percentage quoted by the Office is dramatically lower than a real estimate because a 20,000 member genus is based upon ***all*** of the known human genes in the genome rather than those currently known to be differentiation-specific antigens of epithelial cells. A more realistic estimate should be based upon the number of differentiation-specific antigens which are known to be expressed in epithelial cells.

Given that the term is accepted by those skilled in the art and a diverse and representative number of species are disclosed, the written description of the genus is provided sufficient to establish to those skilled in the that Applicants were in possession of the claimed invention at the time the application was filed.

Applicants respectfully request that the rejection of claims 1, 4, 6–11, 13–15 and 37–47 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 1, 4, 6–11, 13 and 37–45 stand rejected under 35 U.S.C. §103(a) as being unpatentable over T'so (U.S. Patent No. 5,962,237) in view of Eliot (U.S. Patent No. 5,885,574).

T'so discloses removal of white blood cells from a blood sample prior to detection of mRNA encoding PSA or PSMA to reduce false positives.

Eliot describes elimination of CD34+ cells from a sample using an anti-CD34 antibody based kit.

It is asserted it would have been obvious to modify the method of T'so to remove CD34+ cells using the kit disclosed in Eliot rather than removing white blood cells. Applicants respectfully disagree.

While it is true that CD34+ cells are a component of white blood cells they are a very small fraction, i.e. approximately 0.25% of total white blood cells. Nothing in Ts'o or Eliot suggest that CD34+ cells are the source of the false positives that are eliminated when Ts'o eliminates all white blood cells. One would have to know that the CD34+ cells are the source of the false positive in order to modify Ts'o with the teachings of Eliot. Neither reference teaches that the CD34+ cells are the source of the false positive. Accordingly, there would be no expectation of success that eliminating a specific subpopulation that consistutes $1/400^{th}$ of the total cells removed by Tts'o would yield the same result.

Applicants' data in the specification establish that the CD34+ cells rather than other fractions contains the mRNA that yields false positives for the several markers tested.

Provided herewith is Eizawa et al (2004) Heart 90:685-686, which in studying CD34+ rates in cardiac patients reports that CD34+ cells make up about 0.25% of total white blood cells in samples from normal control patients.

Claims 1, 4, 6–11, 13 and 37–45 are non obvious in view T'so and Eliot. Applicants respectfully request that the rejection of claims 1, 4, 6–11, 13 and 37–45 under 35 U.S.C. §103(a) as being unpatentable over T'so in view of Eliot be withdrawn.

Claims 14, 15, 46 and 47 stand rejected under 35 U.S.C. §103(a) as being unpatentable over T'so (U.S. Patent No. 5,962,237) and Eliot (U.S. Patent No. 5,885,574) and further in view of Waldman et al.

Ts'o and Eliot are discussed above..

Waldman et al discloses GCC as a marker for colorectal cancer.

Waldman does not make up for the deificiency of the combination of Ts'o and Eliot. Waldman does not suggest that CD34+ cells are the source of the false positives in the method of Ts'o. None of the reference teaches that the CD34+ cells are the source of the false positive. Accordingly, there would be no expectation of success that eliminating a specific subpopulation that consistutes $1/400^{th}$ of the total cells removed by Tts'o would yield the same result.

Claims 14, 15, 46 and 47 are non obvious in view T'so and Eliot in view of Waldman. Applicants respectfully request that the rejection of claims 14, 15, 46 and 47 under 35 U.S.C. §103(a) as being unpatentable over T'so and Eliot in view of Waldman be withdrawn.

Conclusion

The examination of these claims and passage to allowance are respectfully requested. A Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at 610.640.7855 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any debit or credit any overpayment to Deposit Account No. 50-0436.

Respectfully Submitted,

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